1. A method for generating an adenoviral vector comprising welding together two nucleic acid molecules wherein said two nucleic acid molecules comprise partially overlapping sequences capable of combining with one another allowing the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid of interest or functional parts, derivatives and/or analogues thereof.

2. A method for generating an adenoviral vector comprising welding together, through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said overlapping sequences allow essentially only one homologous recombination which leads to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal and a nucleic acid of interest or functional parts, derivatives and/or analogues thereof.

3. A method according to claim 1 or claim 2, wherein both of said nucleic acid molecules comprise only one adenovirus inverted terminal repeat or a functional part, derivative, and/or analogue thereof.

4. A method according to any one of claims 1-3, wherein said welding together is performed in a cell or a functional part, derivative, and/or analogue thereof.

5. A method according to claim 4, wherein said cell is a mammalian cell.

6. A method according to claim 5, wherein said nucleic acid molecules are not capable of replicating in said mammalian cell prior to said welding together.

7. A method according to any one of claims 1-6, wherein one of said nucleic acid molecules is relatively small and the other is relatively large.

8. A method according to any one of claims 1-7, wherein at least one of said nucleic acid molecules provided to said cell comprises an adenovirus inverted terminal repeat which, on one side, is essentially free of other nucleic acid.

9. A method according to claim 8, wherein said adenovirus inverted terminal repeat is made essentially free of other nucleic acid on one side using a restriction enzyme.

10. A method according to claim 9, wherein said restriction enzyme acts on a site which is not present in adenoviral vector nucleic acid in said nucleic acid molecule.

11. A method according to any one of claims 4-10, wherein the nucleic acids present in said cell do not comprise sequence overlap that can lead to the formation of replication competent adenovirus.

12. A method according to any one of claims 4-11, wherein the chromosomal nucleic acid in said cell comprises at least a functional part of an adenoviral E1-region, or a functional derivative, and/or analogue thereof.

13. A method according to any one of claims 4-12, wherein said cell is a PER.C6 cell (ECACC deposit number 96022940) or a functional derivative, and/or analogue thereof.

14. A method according to any one of claims 4-13, wherein said nucleic acid in said cell further comprises a nucleic acid encoding an adenoviral E2-region and/or an adenoviral E4-region protein.

15. A method according to any one of claims 1-14, wherein at least one of said nucleic acid molecules is linear.

16. A method according to any one of claims 1-15, wherein at least one of said molecules comprises adenoviral capsid protein encoding nucleic acid derived from two different adenovirus serotypes.

17. A method according to any one of claims 1-16, wherein said welding together of said nucleic acid molecules leads to the generation of a physically linked nucleic acid comprising at least two functional adenovirus inverted terminal repeats, a functional encapsulation signal, a nucleic acid encoding at least one adenoviral E1-region protein, at least one adenoviral E2-region encoded protein and/or at least one adenoviral E4-region encoded protein and a nucleic acid of interest or functional parts, derivatives and/or analogues thereof and wherein at least one of said E1-region encoded proteins is under transcriptional control of a conditionally active promoter.

18. A recombinant nucleic acid deposited at the ECACC under No. P97082122, No. P97082119, No. P97082117, No. P97082114,

No. P97082120, No. P97082121, No. P97082116, No. P97082115 or No. P97082118 or a functional part, derivative, and/or analogue thereof.

19. A recombinant nucleic acid pWE/Ad.AflII-EcoRI, pAd5/CLIP, pAd5/L420-HAS, pBS.Eco-Eco/ad5ΔHIIIΔgp19KΔXbaI, pMV/L420-H, pMV/CMV-LacZ, pWE/Ad.Δ5', pWE/AAV.Δ5', pWE/Ad-H.

20. A recombinant nucleic acid comprising:

adenovirus derived nucleotides 1-454 and adenovirus nucleotides 3511-6095 shown in Figures 21 and 22.

21. A recombinant nucleic acid comprising:

a deletion in an E3 region of a recombinant nucleic deposited at the ECACC under No. P97082122, No. P97082119, No. P97082120, No. P97082116.

22. A recombinant nucleic acid according to claim 21, wherein said deletion comprises a gp19K region.

23. A recombinant nucleic acid comprising:

a nucleotide sequence based on or derived from an adenovirus, wherein said nucleotide sequence comprises sufficient adenovirus sequences necessary for replication and capsid gene expression, wherein said nucleotide sequence comprises a deletion of at least the E1 region and encapsulating signal of said adenovirus.

24. A recombinant nucleic acid comprising:

a nucleotide sequence based on or derived from an adenovirus, wherein said nucleotide sequence comprises sufficient adenovirus sequences necessary for replication and

capsid gene expression, and a complementary sequence to an upstream part of the same strand of said nucleic acid, wherein said complementary sequence can base-pair with said upstream part so that it functions as a start-site for a nucleic acid polymerase, wherein said nucleotide sequence comprises a deletion of one Inverted Terminal Repeat, the E1 region and the encapsulating signal of said adenovirus.

25. A recombinant nucleic acid comprising:

a nucleotide sequence based on or derived from an adenovirus, wherein said nucleotide sequence comprises a sequence for adenovirus-independent replication, and sufficient adenoviral sequences necessary for replication, wherein said nucleotide sequence comprises at least a deletion of the E1 region and encapsulating signal of said adenovirus.

26. A recombinant nucleic acid according to claim 25, wherein said nucleotide sequence further comprises a deletion of at least one of the Inverted Terminal Repeats of said adenovirus.

27. A recombinant nucleic acid according to claim 25 or claim 26, wherein said sequence for adenovirus-independent replication comprises an SV40 origin of replication.

28. A recombinant nucleic acid according to any one of claims 18-27 wherein said nucleotide sequence comprises no sequences which allow for homologous recombination leading to replication competent virus in a cell into which said recombinant nucleic acid is transferred.

29. An adapter plasmid comprising:

a nucleotide sequence based on or derived from an adenovirus, wherein said nucleotide sequence comprises in operable configuration at least one functional Inverted Terminal Repeat, one functional encapsulating signal and adenoviral sequences which allow for homologous recombination and the generation of a replication-defective, recombinant adenovirus genome.

30. An adapter plasmid according to claim 29, comprising no sequences which allow for homologous recombination leading to replication competent virus in a cell into which said adapter plasmid is transferred.

31. An adapter plasmid according to claim 30, having no E1 region sequences.

32. An adapter plasmid according to any one of claims 29-31, further comprising a nucleic acid of interest such as a multiple cloning site and/or a transgene.

33. A recombinant nucleic acid according to any one of claim 18-28 or an adapter plasmid according to any one of claims 29-32, wherein said transgene is operatively linked to an E3 promoter.

34. A method for generating recombinant adenovirus having an E1 deletion and a gp19K deletion, comprising the steps of:

growing a cell comprising adenovirus complementing sequences transfected with

i) an adapter plasmid comprising a first nucleotide sequence based on or derived from an adenovirus, wherein said nucleotide sequence comprises in operable configuration one

functional Inverted Terminal Repeat, one functional encapsulating signal and adenoviral sequences which allow for homologous recombination leading to the generation of a replication-defective, recombinant adenovirus genome in a cell into which said adapter plasmid is transferred and having no E1 region sequences, and

ii) a recombinant nucleic acid comprising at least one second nucleotide sequence based on or derived from an adenovirus, wherein said at least one second nucleotide sequence comprises one Inverted Terminal Repeat and sufficient adenovirus sequences for replication and a partial overlap with said adapter plasmid, wherein said at least one second nucleotide sequence comprises a deletion of at least the E1 region, encapsulating signal and gp19K sequences;

wherein said complementing sequences, said first nucleotide sequence and said at least one second nucleotide sequence have no overlapping sequences which allow for homologous recombination leading to replication competent virus,

under conditions wherein recombinant adenovirus having an E1 deletion and a gp19K deletion is generated.

35. A method according to claim 34, wherein said adapter plasmid further comprises a first heterologous nucleotide sequence inserted into said E1 region deletion and said recombinant nucleic acid further comprises a second heterologous nucleotide sequence inserted into said gp19K region.

36. A method for generating recombinant adenovirus, comprising the steps of:

growing a cell comprising adenovirus complementing sequences transfected with

i) a first recombinant nucleic acid comprising a first nucleotide sequence based on or derived from an adenovirus, wherein said first nucleotide sequence comprises a functional encapsulating signal and two functional Inverted Terminal Repeats or functional fragments or derivatives thereof, and wherein said first recombinant nucleic acid has no functional adenoviral genes and

ii) a second recombinant nucleic acid comprising a second nucleotide sequence based on or derived from an adenovirus, wherein said second nucleotide sequence comprises sufficient adenovirus sequences for replication, wherein said second nucleotide sequence comprises a deletion of at least the E1 region and encapsulating signal of said adenovirus;

wherein, said complementing sequences, said first nucleotide sequence and said second nucleotide sequence have no overlapping sequences which allow for homologous recombination leading to replication competent virus,

under conditions wherein recombinant adenovirus is generated.

37. A method for generating recombinant adenovirus, comprising the steps of:

growing a cell comprising adenovirus complementing sequences transfected with

i) a first recombinant nucleic acid comprising a first nucleotide sequence based on or derived from an adenovirus, wherein said first nucleotide sequence comprises a functional encapsulating signal and two functional Inverted Terminal Repeats or functional fragments or derivatives thereof, and wherein said first recombinant nucleic acid has no functional adenoviral genes and

ii) a second recombinant nucleic acid comprising a second nucleotide sequence based on or derived from an adenovirus, wherein said second nucleotide sequence comprises a sequence for adenovirus-independent replication, and sufficient adenoviral sequences necessary for replication, wherein said second nucleotide sequence comprises at least a deletion of the E1 region and encapsulating signal of said adenovirus;

wherein, said complementing sequences, said first nucleotide sequence and said second nucleotide sequence have no overlapping sequences which allow for homologous recombination leading to replication competent virus,

under conditions wherein recombinant adenovirus is generated.

38. A method according to claim 37, wherein said cell comprises at least one nucleic acid molecule wherein said cell expresses SV40 Large T antigen proteins or functional fragments thereof.

39. A method according to claim 37 or claim 38, wherein said second recombinant nucleic acid molecule is replicated.

40. A replication defective adenovirus comprising:

a genome based on or derived from an adenovirus, wherein said genome comprises at least a functional encapsulating signal and two functional Inverted Terminal Repeats or functional fragments or derivatives thereof and wherein said genome comprises no functional adenoviral genes and has no overlapping sequences which allow for homologous recombination leading to replication competent virus in a cell into which said replication defective adenovirus is transferred.

41 A replication defective adenovirus according to claim 40, further comprising:

one or more nucleic acids of interest.

42. A non-human cell comprising a genome of a replication defective adenovirus according to claim 40 or claim 41..

43. A non-human cell according to claim 42, wherein said cell is a mammalian cell.

44. A method for transducing a cell, comprising the step of:

contacting said cell with a replication defective adenovirus according to claim 40 or claim 41 under conditions wherein said cell is transduced.

45. A non-human cell produced according to the method of claim 44, wherein said cell is a mammalian cell.

46. A method for generating recombinant adenovirus comprising the step of:

growing a cell comprising adenovirus complementing sequences and

i) a first recombinant nucleic acid comprising a first nucleotide sequence based on or derived from an adenovirus, wherein said first nucleotide sequence comprises a functional encapsulating signal and two functional Inverted Terminal Repeats or functional fragments or derivatives thereof, and wherein said first recombinant nucleic acid has no functional adenoviral genes and,

ii) a second recombinant nucleic acid comprising a second nucleotide sequence based on or derived from an

adenovirus, wherein said nucleotide sequence comprises at least all adenovirus sequences, or functional fragments or derivatives thereof necessary for replication and capsid gene expression, and a complementary sequence to an upstream part of the same strand of said nucleic acid, wherein said complementary sequence can base-pair with said upstream part so that it functions as a start-site for a nucleic acid polymerase, wherein said second nucleotide sequence comprises a deletion of one Inverted Terminal Repeat, the E1 region and the encapsulating signal of said adenovirus;

wherein, said complementing sequences, said first nucleotide sequence and said second nucleotide sequence have no overlapping sequences which allow for homologous recombination leading to replication competent virus,

under conditions wherein recombinant adenovirus is generated.

47. A cell comprising a recombinant nucleic acid according to any one of claims 18-28, 33 or a replication defective adenoviral vector according to any one of claims 40, 41, 55 or 56 and/or an adapter plasmid according to any one of claims 29-32.

48. A method for the replacement of a defective gene in a host cell genome comprising the step of:

growing said host cell with a recombinant nucleic acid molecule derived from a replication defective adenovirus comprising a functional version or part thereof of said defective gene under conditions wherein at least one allele of said defective gene in said host cell genome is replaced.

49. A method according to claim 44, wherein said replication defective adenovirus expresses no adenoviral genes.

50. A method according to claim 44, wherein said-defective gene is a defective tumor suppressor gene.

51. An isolated cell comprising a genome of a replication-defective adenovirus according to any one of claims 40, 41, 55 or 56.

52. A isolated cell according to claim 51, wherein said cell is a human cell.

53. A recombinant nucleic acid according to any one of claims 18-28, wherein said deletion in the E3 region is replaced with a transgene.

54. A method according to claim 34 or claim 35, wherein said at least one second nucleotide sequence comprises a first and second molecule wherein said first molecule has said partial overlap with said adapter plasmid at the 3' end, and said second molecule comprises said Inverted Terminal Repeat and region including deletion of said gp19K sequences.

55. A replication-defective adenovirus comprising:
a genome based on or derived from an adenovirus, wherein said genome comprises a first deletion in an E1 region and a second deletion in a gp19K region.

56. A replication-defective adenovirus according to claim 55, wherein transcription of said transgene is directed by an E3 promoter.

57. An isolated cell comprising:
a recombinant nucleic acid according to any one of claims 18-28, or 33 or a replication defective adenoviral vector according to any one of claims 40, 41, 55 or 56 and/or an adapter plasmid according to any one of claims 29-32.

58. The isolated cell of claim 57 wherein said cell is a human cell.